

REMARKS

In the Office Action dated March 22, 2004, in response to Applicant's arguments, the Examiner withdrew her rejection of claims 1-6 and 14 under 35 U.S.C. 102(b), and claims 7-13 and 15 under 35 U.S.C. 103(a). However, the Examiner has cited new grounds of rejection, Popow et al. Respiration 1988; 54:132-132 ("Popow et al."), and Sessa et al., J. Chromatography, 382(1986)258-263 ("Sessa et al.") and withdrawn the allowability of claims 1-15 in the present application.

Applicant has presented amended claims 1, 4-7 And 13 with the limitation "endogenic" and also added new claims 20-34 directed to analytical methods for use in determining development or progression of a disease or the effect of a treatment on the progression of a disease in a body fluid or tissue sample. As to the addition of the term "development," support can be found in the specification on page 3, first full paragraph.

Rejection under 35 U.S.C. § 102(b)

In the Office Action dated March 22, 2004, the Examiner rejected claims 1-6 under 35 U.S.C. §102(b) as being anticipated by Popow et al. The Examiner stated that

the reference discloses a biochemical analysis of 3-cis-hydroxyproline, 4-cis-hydroxyproline and its isomers in collagen. Applicant suggests that the reference only teaches detection of isomers of cis-hydroxyproline that have been added exogenously by the authors either by feeding the animals the compounds of interest or through addition of the compounds of interest to the analytical samples as an internal standard. Applicant has amended claims 1, 4-7 and 13 and added the limitation "endogenic" to these claims, thereby obviating the rejection, and respectfully request the Examiner's rejection be withdrawn.

Rejection under 35 U.S.C. § 102(b)

The Examiner also rejected claims 1-6 and 14 under 35 U.S.C. §102(b) as being anticipated by Sessa et al. The Examiner states that upon re-reading this reference, the Examiner concludes that because the quantization of total hydroxproline was determined by comparing the ratio of t-4-Hyp/c-4-Hyp peak heights in the chromatogram, it anticipates the claimed invention. Applicant respectfully traverses.

In our previous response of July 28, 2003, at page 8, we discussed that the use of the c-4-Hyp in the

paper was an internal standard. Applicant maintains that this is still the case.

The purpose of an internal standard in HPLC is to allow the investigator to quantify an amount of unknown analyte (t-4-Hyp) by spiking a sample with an internal (meaning in the sample itself) standard that appears in the chromatogram in a convenient proximity to where the analyte should appear (which is determined by injecting known quantities of analyte and making a standard curve). The amount of internal standard (c-4-Hyp) added is known and is the same in every sample. The one most important aspect of an internal standard is that it is not found endogenously in the samples endogenously that are being spiked. When the analysis is performed, the investigator can determine the unknown amount of t-4-Hyp based on the ratio of the peak height of the t-4-Hyp to the known amount of the c-4-Hyp peak. The internal standard cannot work if there is some unknown quantity of the same compound as the internal standard is derived from the sample tissue as well.

Applicant respectfully points out that nowhere in Sessa et al. do they state that c-4-Hyp is made endogenously in either of the tissues sampled. It has been general knowledge that c-4-Hyp was not present in every type of collagen. This is why Sessa et al. used c-4-Hyp as the internal standard. Applicant suggests that the Examiner may have confused two measurements discussed in the reference, the measurement of t-4-Hyp and the measurement of total hydroxyproline. In regard to the latter, Applicant submits that the authors only performed standard curves for t-4-Hyp and proline to identify total *trans*-hydroxyproline as a proportion of total proline, because the authors did not expect to see c-4-Hyp in their samples (Sessa et al., page 262). That is why there is no standard curve for c-4-Hyp anywhere in the reference, and that is also why c-4-Hyp is never mentioned again except when used as an internal standard (page 259).

Notwithstanding the above, Applicant's amendment of claims 1, 4-7 and 13 above to add the limitation "endogenic", obviates this rejection. Applicant respectfully requests the Examiner's rejection be withdrawn.

Rejection under 35 U.S.C. § 103(a)

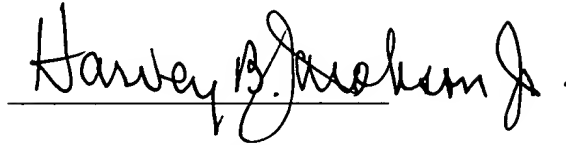
The Examiner rejected claims 7-13 and 15 as being unpatentable over Sessa et al. (J. Chromatog. 382(1986) 258-263). Applicant submits that for the reasons stated with regard to this reference above apply to this rejection as well. Sessa et al. do not teach measurement of c-4-Hyp and therefore cannot render the newly amended claims as obvious. In view of the amended claims, the rejection should properly be withdrawn as moot. Pending claims 1-15 and 20-34 are now properly in condition for allowance.

Request for Interview

Applicant respectfully requests either a telephonic or an in-person interview should there be any remaining issues.

Applicant respectfully requests entry of this amendment. If there are any questions, the Examiner is invited to call the attorney at 202-638-6666.

Respectfully submitted,
JACOBSON HOLMAN PLLC

A handwritten signature in black ink, reading "Harvey B. Jacobson", written over a horizontal line.

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